Familial Occurrence of Spontaneous Dissection of the Internal Carotid Artery

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Spontaneous dissections of the extracranial internal carotid artery are diagnosed more frequently as their clinical and angiographic features are more widely recognized. Familial occurrence of spontaneous dissection of the internal carotid artery has not been previously reported. We describe the occurrence of this entity in a mother and daughter and also in a father and son. The familial occurrence of spontaneous dissection of the internal carotid artery raises the possibility of an inherited disorder of the blood vessel wall that predisposes the artery to this disorder. Fibromuscular dysplasia is suspected to be the underlying arterial disease, but other unknown arteriopathies cannot be excluded. (Stroke 1987;18:246-251)

Subjects and Methods

CASE 1. Severe left occipital headache, hoarseness, and dysphagia developed in a 47-year-old, right-handed man in early January 1983. He also had intermittent nausea and light-headedness and was found to be hypertensive. He was treated with analgesics for pain, a diuretic for hypertension, and antibiotics for presumed sinusitis. The dysphagia and hoarseness became more prominent, and 2 weeks later he noted drooping of the left upper lid. Several studies were performed, including computed tomographic (CT) scan of the head, metrizamide cisternography, jugular venography, and bilateral carotid and right vertebral angiography. The patient was referred to the Mayo Clinic because of the suspicion of a tumor high in the right side of the neck.

The neurologic examination on January 8, 1983, revealed a left Horner’s syndrome, left vocal cord paralysis, and weakness of the palate, tongue, and sternocleidomastoid muscle on the left. Results of the rest of the neurologic examination were normal. The findings pointed to involvement of the 9th–12th cranial nerves on the left side and a left Horner’s syndrome without any long track signs. Review of the previous CT scan and metrizamide cisternogram revealed only a mild shift of the spinal cord from the left to the right without evidence of a space-occupying lesion on the left. The jugular venogram was normal. The arteriograms, however, demonstrated bilateral dissections of the distal portions of the cervical ICA’s. On the left, the vessel was dilated and tortuous at the base of the skull, where a small aneurysm was also noted. The vertebral angiogram was normal. Cerebrospinal fluid examination revealed 23 leukocytes/mm³ (17 lymphocytes, 4 polymorphonuclear leukocytes, and 2 monocytes), a protein value of 55 mg/dl, and normal glucose. These changes were thought to be related to the patient’s previous metrizamide study.

In view of the patient’s history of progressing neurologic deficits and uncertainty about the relation between the carotid dissection and the symptoms, a combined exploration (through a suboccipital craniectomy and upper cervical incision) was performed. The clinically involved cranial nerves were identified, and they were free of any tumor infiltration and were grossly normal. Within 2 months he began to show improvement. The headaches resolved. The dysphonia and ptiosis disappeared within 8 months. There was mild residual dysphagia, which was eliminated by a cricopharyngeal myotomy. At last follow-up, about 2½ years later, the patient was asymptomatic.

CASE 2. In early January 1983, throbbing right-sided pain developed in the cheek, upper jaw, and orbital and periorbital regions of a 76-year-old, right-handed man, the father of Patient 1. Maximal on the first day, the pain on subsequent days became less severe but was persistent and fluctuated in intensity. About 2 weeks later, when the right-sided head and face pain had become intermittent, the patient noted horizontal diplopia. In early February 1983, the patient was examined at the Mayo Clinic, by which time the diploia had resolved.

On examination there was miosis on the right. Mild-to-moderate peripheral left facial weakness was noted, a residual of Bell’s palsy that had occurred 6 years earlier. No cervical or cephalic bruits were found. Funduscopic examination showed only hypertensive ves-
sel changes but no retinal emboli. Brachial blood pressure was 144/92 mm Hg. The results of a CT scan of the head and cerebrospinal fluid examination were normal. A right brachial angiogram (Figure 2) showed luminal irregularity with the formation of a small aneurysm above a cervical loop of the right ICA, a finding suggestive of dissection. The right carotid bifurcation was normal. The right-sided miosis and head and face pains resolved within 2 months.

Case 3. In early June 1975, a 35-year-old, right-handed woman developed right-sided ear, neck, face, and head pain and became aware of a small pulsatile mass in the right side of her neck and a loud bruit over the entire right side of her head. On July 2, transfemoral bilateral carotid and vertebral cerebral angiography demonstrated occlusion of the left ICA at its origin (Figure 3A) and a subcranial aneurysm of the right ICA with an adjacent stenosis of the ICA extending into the carotid canal (Figure 3B). Luminal irregularities in the vertebral arteries at C-2 were suggestive of (although not diagnostic of) fibromuscular dysplasia.

On follow-up, the right-sided headaches had resolved, although occipital bifrontal tension headaches were frequent. The subjective bruit had decreased and was audible only in a quiet room or after exercise. A slight ptosis on the right was the only abnormality found on examination. Transfemoral bilateral carotid and vertebral angiography in May 1976 showed considerable improvement. Only mild tortuosity and minimal luminal irregularities of the right ICA persisted in the carotid canal. The subcranial aneurysm had significantly decreased in size. The occlusion of the left ICA remained unchanged. The vertebral arteries were normal. The patient remained normotensive.

In early June 1983, at age 43 years, the patient had experienced abrupt left flank pain that later extended to the groin and anterior aspect of the thigh on the left and was associated with nausea. Findings on examination included microhematuria and blood pressure of 180/120 mm Hg. After several days, a similar pain also developed on the right side. Transfemoral abdominal aortography and bilateral renal angiography on June 18, 1983, demonstrated dissection involving the main renal artery that extended into the 2 major primary branches and high-grade stenosis at the bifurcation. In addition, irregularity of the right main renal artery was found that also involved primary and secondary branches.

The patient's hypertension was controlled with anti-hypertensive agents. The headaches, flank pain, nausea, and vomiting resolved within 2 weeks. Repeat abdominal aortography and bilateral renal arteriography in October 1983 demonstrated intimal irregularities in the aorta distal to the takeoff of the renal arteries. The right kidney had a small 4- by 5-mm aneurysm in the middle portion and a cortically based wedge-shaped area of infarction at the junction of the middle and lower poles. The left renal artery was narrowed at the bifurcation of the branches to the upper and lower poles. The patient has remained essentially asymptomatic.
FIGURE 3. (Case 3) (left) Left carotid arteriogram demonstrates occlusion (arrow) of internal carotid artery at its origin. (right) Right carotid arteriogram shows subcranial dissecting aneurysm (arrow) and narrowing of internal carotid artery distal to aneurysm and extending into carotid canal.

Discussion

The pathogenesis of spontaneous dissection of the ICA has not been definitely established. Although such dissections are called "spontaneous," the role of minor or trivial trauma has not been entirely excluded by some authors. Some cases have evidence for a primary arterial disease. Spontaneous carotid dissection has been noted in association with Marfan's syndrome. Angiographic changes of fibromuscular dysplasia have been noted in the ICA's or in the vertebral or renal arteries of about 15% of affected patients. However, the actual frequency may be even higher because the changes related to dissection may distort or obliterate the angiographic changes of fibromuscular dysplasia in the same vessel. Furthermore, in some patients, the angiographic changes of fibromuscular
dysplasia may be subtle and may thus go undiagnosed. Subtle intimal irregularities of unclear significance, remote from the site of dissection, are also noted in some cases. Whether these are a *forme fruste* of fibromuscular dysplasia or another form of arteriopathy or neither must await histologic confirmation. Wirth et al described a single irregularity that proved to be a form of fibromuscular dysplasia. We have seen subtle intimal irregularities, remote from the dissection, that have disappeared in follow-up angiograms. Such cases have been classified as idiopathic regressing arteriopathy, pending histologic studies. Cystic medial necrosis has been described, especially in early reports that were based on autopsy results. Many of the
more recent reports, primarily based on surgical specimens, have failed to show any particular microscopic abnormalities in the vessels that have been studied.

Clearly, patients with spontaneous dissections of the ICA have a higher incidence of hypertension. The role of contraceptive medications, smoking, or migraine is unclear. Atheromatous changes are only uncommonly found in ICA's involved by dissection. Of interest is the fact that carotid dissection rarely recurs in the same vessel. Spontaneous dissection of the ICA likely has a multifactorial pathogenesis, and both mechanical factors and an underlying disorder of the blood vessel wall contribute to the disorder in many cases.

The familial occurrence of spontaneous dissection of the ICA raises the possibility of an inherited disorder of the blood vessel wall that predisposes the artery to spontaneous dissection. Our first patient (Case 1) had bilateral dissections of the ICA. The clinical manifestations were all left-sided. We could explain the left Horner's syndrome and left hemicrania on the basis of the dissection, but we had difficulty explaining the lower cranial nerve palsies on the basis of the dissection, especially in view of the history of progression; thus, surgical exploration was performed. Lower cranial nerve palsies in association with dissections of the cervical segment of the ICA, however, have been reported previously. Havelius et al reported unilateral lower cranial nerve palsies (9th—12th) in a patient with what seems to have been bilateral dissections of the ICA's on a background of fibromuscular dysplasia. Goodman et al noted hemilingual paralysis in a patient with spontaneous dissection of the ICA. This patient also had ipsilateral oculosympathetic palsy. Of the 5 cases of dissection of the ICA reported by Bradac et al, one had ipsilateral Horner's syndrome and hemi-lingual paralysis. Another patient had ipsilateral oculosympathetic palsy and paralysis of the lower cranial nerves (9th—12th).

In our second patient (Case 2), the transient horizontal diplopia could not be definitely explained. However, the right-sided headache and face pain and oculosympathetic paresis seemed to be related to the extracranial dissection of the right ICA. In the angiograms of Cases 1 and 2 (the father and son), we found no definite clues for an underlying arterial disease such as fibromuscular dysplasia. It was interesting that the symptoms in both patients had developed in January 1983. However, we could not blame an environmental factor because the patients lived in different states and far from each other. The occurrence of spontaneous bilateral dissection of the ICA in the son raises the possibility of the presence of an underlying arterial disease, and the occurrence of the dissection in the father suggests that this disease might have a hereditary tendency. Whether this underlying arterial disease is a forme fruste of fibromuscular dysplasia or another arteriopathy remains undetermined.

Case 3 in this article was initially reported in 1977 as 1 of the 3 cases described as idiopathic regressing arteriopathy. In this case not only the angiographic changes related to the dissection had improved in the subsequent angiograms but also the luminal irregularities of the vertebral arteries (not involved by dissection) had disappeared in the follow-up angiograms. Eight years later, spontaneous dissections of both renal arteries developed, suggesting the presence of a more diffuse arteriopathy. Although fibromuscular dysplasia was suspected, another undetermined arteriopathy could not be excluded.

We have not yet had the opportunity to examine histologically the intimal irregularities that are remote from the dissection and are not typical of fibromuscular dysplasia on angiography. However, the patients with such angiograms are more likely to be female and more likely to have involvement of the vertebral arteries. Despite having many reservations without pathologic confirmation, we suspect that such remote intimal irregularities may be a forme fruste of fibromuscular dysplasia.

The arteriogram of the third patient's daughter (Case 4) showed typical changes of dissection of the ICA. However, the other vessels visualized in this arteriogram were entirely normal without evidence of any luminal irregularities. On follow-up, only an IV-DSA was available, which showed resolution of the stenosis of the right ICA. However, subtle intimal irregularities in this vessel, if present, might have been missed. The occurrence of multivessel dissections in the mother strongly suggests a fairly diffuse arteriopathy. The dissection occurring in her daughter raises the possibility that this arteriopathy might be inherited. In the mother, fibromuscular dysplasia has been suspected but not confirmed histologically. The daughter may have a forme fruste of this disease that has not caused any detectable angiographic findings. Alternatively, they may have a different type of arteriopathy. A less likely possibility is that the occurrence of dissection in this mother and daughter was coincidental.

As reviewed by Petit et al, familial fibromuscular dysplasia of the renal arteries has been described in 2 sisters, 33 2 twin sisters and 2 brothers, a mother and daughter, 32 2 female cousins of 2 twin sisters, and probably in 2 brothers and their 2 sisters. In 1965, Halpem and associates raised the possibility of a congenital or hereditary nature for fibromuscular dysplasia. In 1980, Rushton analyzed the study of families of 20 patients with fibromuscular dysplasia and concluded that it could be a hereditary disease transmitted as an autosomal dominant trait with variable penetrance. Mettinger reviewed 1,100 cases of fibromuscular dysplasia from the literature, including 300 cases with aortocranial lesions, and suspected that the disease was inherited as a dominant trait with reduced penetrance in males. Mettinger and Ericson reviewed the genetic characteristics of fibromuscular dysplasia in 37 cases they had selected from a pool of 4,000 angiograms of carotid or vertebral arteries. The clinical manifestations of some of their patients as described, however, are reminiscent of carotid dissection. They concluded that in most cases fibromuscular dysplasia is inherited as an autosomal dominant trait with reduced penetrance in males. Petit
et al., in a report on the familial form of fibromuscular dysplasia of the ICA, described a 32-year-old woman with dissection of the ICA on the left and angiographic changes typical of fibromuscular dysplasia of the ICA on the right. In this patient’s father, 23 years earlier, occlusion of the left ICA had developed, which the authors presumed to have been related to fibromuscular dysplasia.

None of the 4 patients had a history of relevant trauma, and no environmental factor could be determined. The familial occurrence of spontaneous dissection of the ICA seems to point to an underlying arterial disease with a hereditary tendency that predisposes the vessel to spontaneous dissection in some cases. Fibromuscular disease may be the underlying arterial disease, but the possibility of other undetermined arteriopathies cannot be excluded.

References

9. Austin MB, Schaeffer RF: Marfan’s syndrome, with unusual blood vessel manifestations: Primary mediocroneous dissection of right innominate, right carotid, and left carotid arteries. Arch Pathol 1957;64:205–209

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